Claims

What is claimed is:

1. A composition comprising,

a protein portion, wherein the protein portion contains a substituted cysteine residue at a desired location to be tagged;

a tail portion at the terminal end of the protein portion; and

a knob, wherein the knob is located at the free terminal end of the tail portion and contains a cysteine residue, and wherein the cysteine residue of the knob is capable of forming a disulfide with the substituted cysteine in the protein portion.

2. The composition of claim 1, wherein the tail contains a protease cleavage site.

3. The composition of claim 1, wherein the knob comprises an epitope tag.

4. The composition of claim 1, wherein the knob comprises a polypeptide.

5. The composition of claim 1, wherein the knob comprises a protein.

6. The composition of claim 5, wherein the knob cysteine is located on the surface of the protein.

7. The composition of claim 1, wherein the protein portion is a monomeric protein.

8. The composition of claim 1, wherein the protein portion is a multimeric protein.

9. A method for tagging a protein at a specific site comprising,

a) selecting a desired protein;

b) locating a specific site on the desired protein to be tagged;

c) selecting a desired knob, wherein the desired knob contains a cysteine residue;

d) preparing a construct encoding the desired protein, a tail portion and the desired knob, wherein the desired protein has a cysteine residue substituted at the site to be tagged;

e) inserting the construct into a cell for expression of the tagged protein, wherein the cysteine in the knob and the substituted cysteine in the desired protein form a disulfide bond.

10. The method of claim 9, wherein the knob comprises an epitope tag, a signal sequence or a protein.

11. The method of claim 10, wherein the knob protein is a protease.

12. The method of claim 9, wherein the desired protein is monomeric.

13. The method of claim 9, wherein the desired portein is multimeric.

14. A protein purification method comprising,

a) inserting a construct capable of expression in a cell, wherein the construct encodes a protein, wherein the protein comprises a cysteine residue substituted at a desired site to be tagged, a tail portion at the terminal end of the protein, wherein the tail portion contains a protease cleavage site, and a knob at the end of the tail portion, wherein the knob contains a cysteine residue;

b) lysing the cell;

c) purifying the protein based on the characteristics of the knob.

15. A method for tagging hCG comprising,

a) preparing a construct capable of expressing native hCGβ or hCGβ-S138C;

b) preparing a construct capable of expressing native hCGα or hCGα cysteine substituted analogs;

c) inserting the constructs of step a) and b) into COS-7 cells for co-expression.

16. The method of claim 15, wherein the construct of step a) further comprises fusing a protein to residue 140 or 145 of hCGβ.

17. The method of claim 16, wherein the protein is β-lactamase.

18. The method of claim 15, wherein the hCGα cysteine substituted analogs are selected from SEQ ID NO: 1 thru SEQ ID NO: 35.

19. A method for mapping the distance between protein molecules comprising,

a) selecting a first protein molecule;

b) selecting a second protein molecule, wherein the first protein molecule and the second protein molecule interact;

c) producing first protein molecules, wherein each first protein molecule produced contains a knob located at a different site on the first protein;

d) producing the second protein molecule;

e) using the proteins produced in steps c) and d) to analyze the distance between the first protein and the second protein.